In contrast to these clearly semiquantitative results, we found a
direct, logarithmic, and quantitative relationship between E/A
ratio and PA pressure measured as continuous variables in patients
with CTEPH. We also documented a similar direct relationship
between E/A and cardiac output in the same group. The results of
our study expand upon previous studies that have reported on
abnormal LV diastolic function in patients with chronic pulmo-
nary hypertension. However, it is still difficult to hypothesize that
abnormal LV diastolic filling contributes significantly to dyspnea
in these patients. In fact, pulmonary capillary wedge pressure
increased slightly from 9.8 ± 5 to 11.5 ± 4.5 mm Hg (p = 0.04)
after PTE. This suggests that dyspnea in patients with severe
pulmonary hypertension is unlikely to be related to an elevated LV
filling pressure.

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Detrimental Effects of Late Artery Opening
In reference to the recent study by Yousef et al. (1) in the Journal,
we agree that percutaneous coronary interventions (PCI) for an
occluded artery late after an acute myocardial infarction are not
risk-free procedures, and even an immediate angiographic success
may be harmful in the long term. The investigators attribute
detrimental effects of late reperfusion—significantly greater one-
year left ventricular (LV) end-systolic and end-diastolic vol-
umes—to periprocedural microembolization of collateral vessels.
However, as reported in the study limitations, the researchers did
not routinely measure cardiac markers after PCI; therefore, no
proof for such a causative mechanism exists.

An alternative explanation for this finding is that the adverse
effect on remodelling of the invasive strategy is not related to the
PCI procedure itself but to the extremely high rate of late events
occurring in these patients in relation to a suboptimal treatment.
Here the 50% rate of adverse event at one year is far higher than the
32% rate reported after stent implantation in occluded arteries,
even using the now outdated Palmaz-Schatz stents and warfarin
therapy (2). The use of NIR stents (3) and the suboptimal (two
weeks) duration of clopidogrel therapy might be advocated as a
cause of higher-than-expected restenosis and reocclusion rates in
the study by Yousef et al. (1).

Moreover, LV volumes are certainly a better surrogate end point
than exercise tolerance, but improvements in exercise duration and
peak rate-pressure products in the intervention group are unex-
pectedly discordant from echocardiographic findings. Changes in
mitral regurgitation severity may contribute to limitation of exer-
cise capacity (4). The assessment of mitral regurgitation in this
setting could be extremely helpful in clarifying whether detrimen-
tal effects on remodelling are uniformly found in the entire cohort
of patients who underwent PCI or only in the subgroup of patients
who experienced adverse events.

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exercise-induced mitral regurgitation to exercise stroke volume and
exercise capacity in patients with left ventricular systolic dysfunction.

REPLY
Zimarino et al. have based their conclusions on a comparison of
events between the TOAT (1) and GISSOC (2) studies. This
comparison is not justified as neither study was powered to
examine clinical end points. Furthermore, the inclusion criteria of
the trials differed. For example, only 50% of the stented patients
within GISSOC had a prior myocardial infarction, whereas in
TOAT this was 100%. Moreover, to increase the prevalence of
adverse remodelling, the eligibility criteria of TOAT ensured that
the stented vessel subtended a large volume of infarcted myocar-
dium with a presumed high microvascular resistance and thus more
disordered flow. In addition, 28% of events within TOAT com-
prised heart failure and stroke, end points that are unlikely to be
related to reocclusion. Omitting these end points results in a
one-year event rate of 24% in those randomized to intervention,
compared to a nine-month event rate of 32% in the corresponding patients within GISSOC.

Undoubtedly, as stent designs improve, late complications will become less frequent; thus, use of drug-eluting stents (3) in TOAT and GISSOC could have resulted in fewer restenoses and reocclusions. The use of post-stent clopidogrel and other thienopyridines for only two weeks is validated and supported by Mishkel et al. (4) and Berger et al. (5).

Unfortunately, Doppler color flow mapping was not a protocol requirement in our study; therefore, quantitative assessment of resting mitral regurgitation is incomplete. Nevertheless, because all patients had single-vessel disease with left anterior descending artery occlusion, the posterior papillary muscle is likely to have been spared, making annular dilation the most probable mechanism of mitral incompetence. We agree that the increased exercise endurance observed in open-artery patients (despite increased left ventricular volumes) is paradoxical, and likely to be mediated through a placebo effect.

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Specificity of Noninvasive Pacemaker Stress Echocardiography in Diagnosis of Coronary Artery Disease

We read with great interest the recently published study by Picano et al. (1) in the October 2, 2002, issue of JACC. The investigators concluded that noninvasive pacemaker stress echocardiography is a diagnostically efficient method for patients with a permanent pacemaker and suspected or known coronary artery disease (CAD).

Nevertheless, some concerns arise based on our experience and from careful review of the published reports.

First, the main problem in detecting CAD in patients with permanent ventricular pacing is the low specificity of noninvasive techniques related to abnormalities of microvascular flow arising from chronic functional and/or structural abnormalities induced by abnormal ventricular excitation (2). We do not believe that the study by Picano et al. (1) could solve this problem; the studied group consisted of patients with a high prevalence of risk factors for CAD (>50%) and/or previous myocardial infarction (37%): it was, therefore, an excellent way to assess the sensitivity of the method, but not the specificity. In addition, 15 of 45 patients were in AAI pacing mode, and even for the remaining patients we do not know if there was partial or full ventricular excitation from the pacemaker electrode during daily life or during the stress protocol. We also do not know whether the studied group represents a total population of patients with a pacemaker, as the manner of the patients’ recruitment is unclear.

Second, the allegation that perfusion defects are more common than wall motion abnormalities during stress in patients with alterations of coronary flow reserve and normal epicardial coronary arteries conflicts with the findings of a study by Tse et al. (3), who observed wall motion abnormalities by radionuclide ventriculography to occur in the same proportion of patients with permanent ventricular stimulation and no significant CAD as did perfusion defects detected by dipyridamole thallium myocardial scintigraphy. Thus, the advantage of the stress echocardiogram remains in question.

Third, given the deterioration of myocardial perfusion over time that is observed in some studies (3,4), it is crucial to know the mean duration of pacing, especially in patients without wall motion abnormalities. Such data were not provided in the study by Picano et al. (1).

In conclusion, although no one has doubt about the diagnostic accuracy of the noninvasive pacemaker stress echocardiogram in patients with AAI pacing mode, or, more generally, about the sensitivity of the same method in detecting CAD, the specificity of the method remains in doubt. Based on data currently available, a specificity of 50% is the best we can expect from noninvasive techniques (2–5), at least in patients with permanent ventricular stimulation.

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